METHODS OF IMPROVING HEALTH-RELATED QUALITY OF LIFE IN INDIVIDUALS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the priority benefit of U.S. Provisional Application No. 60/436,906, filed December 27, 2002, and U.S. Provisional Application no. 60/478,128, filed June 11, 2003, the contents of both of which are hereby incorporated by reference into the present disclosure.

TECHNICAL FIELD

[0002] This invention relates to the field of antibody-mediated pathologies such as lupus. More particularly, the invention relates to methods of improving or stabilizing the health-related quality of life of individuals with systemic lupus erythematosis.

BACKGROUND OF THE INVENTION

[0003] Systemic lupus erythematosus (SLE) is characterized by multisystem organ involvement and variable disease course including flares and remissions. Renal disease is a primary cause of morbidity and mortality in SLE patients (Pistiner M, et al. (1991) *Semin Arthritis Rheum* 21:55-64, Hochberg MC, et al. (1985) *Medicine* 64:285-295, Dubois EL, et al. (1964) *JAMA* 190:104-11, Vitali C, et al. (1992) *Clin Exp Rheumatol* 10:527-39). In patients with SLE renal disease, high levels of anti-double stranded DNA antibodies (anti-dsDNA) correlate with active glomerulonephritis. A pathogenic role is suggested as these antibodies can be eluted from diseased glomeruli (Winfield JB, et al. (1977) *J Clin Invest* 59:90-6, Hahn, B. (1998) *N Engl J Med* 338:1359-68, Vlahakos DV, et al. (1992) *Kidney Int*

41:1690-700, Ehrenstein MR, et al. (1995) *Kidney Int* 48:705-11, Rothfield NF, et al. (1967) *J Clin Invest* 46:1785-94, Lefkowith JB, et al. (1996) *J Clin Invest* 98:1373-80). Significant increases in anti-dsDNA levels are associated with increased SLE disease activity; sustained reductions in antibody levels have been associated with improved treatment outcomes (Borg EJ, et al. (1990) *Arthritis Rheum,* 33:634-43, Swaak AJG, et al. (1986) *Ann Rheum Dis* 45:359-66, Bootsma H, et al. (1995) *Lancet* 345:1595-9).

[0004] Although overall patient prognosis in SLE has improved, treatment regimens are not ideal and lupus nephritis continues to be associated with relatively poor overall survival as compared to individuals without renal involvement in lupus (Seleznick et al. (1991) *Semin. Arthritis Rheum.* 21:73-80). Acute episodes of nephritis are usually treated with high dose corticosteroids and/or immunosuppressive agents, typically cyclophosphamide, azathioprine, or recently mycophenolate mofetil. Poor tolerability, insufficient efficacy, and toxicity associated with these treatments limit their use, creating a need for alternative therapies (Klippel JH, et al. (1990) *JAMA* 263:1812-5, Ortmann RA, et al. (2000) *Rheum Dis Clin North Am* 26:363-75).

[0005] Synthetic double-stranded oligonucleotides (dsON) have been shown to cross-react with anti-dsDNA antibodies (U.S. Patent No. 5,276,013). The use of dsON conjugated with non-immunogenic carriers, also referred to as platforms, has been proposed for a therapeutic approach for the treatment of SLE. For example, a tetrakis conjugate, LJP 249, composed of four dsON attached to a poly(ethylene glycol) valency platform was used to demonstrate tolerance in an immunized mouse model system (Jones et al. (1994) *Bioconjugate Chem.* 5:390-399).

[0006] LJP 394 (abetimus sodium; also known as Riquent™), composed of 4 deoxynucleotide sequences bound to a triethylene glycol backbone, is a non-immunogenic, immunomodulatory agent, that selectively reduces anti-dsDNA titers in murine models of SLE and in patients with SLE (Plunkett et al. (1995) *Lupus*